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Medical Management of Peptic Ulcer

The problem of peptic ulcer is important in the general economy if only by virtue of the fact that 5 to 10% of the population of this country at some time during their lives will have such a lesion. Fortunately, most of these persons do not experience any serious consequence of the disease and many have little difficulty in controlling its symptoms. However, the morbidity produced by a disease of this magnitude of occurrence makes its recognition vital and calls for intelligent appreciation of the essentials of treatment that render control of the lesion a reasonable possibility.

Were the cause of peptic ulcer more accurately understood, it is likely that its treatment would be more efficacious and less diverse. In a broad sense, two major schools of thought exist with respect to the treatment of ulcer: the first emphasizes a strict ritual of diet, antacid medicine, sedatives, and anticholinergic drugs, whereas the second emphasizes the psychotherapeutic aspects of the problem at the expense of all else. Actually, as long as the cause of peptic ulcer is unknown, it would be unwise to assume too rigid an approach to its treatment because both concepts contain an element of truth that can give promise of aid when they are honestly and intelligently applied.

The concept of the etiologic factors in peptic ulcer is diverse. Trauma, focal infection, vascular lesions, nutritional deficiencies, tissue susceptibility, excessive secretion of acids, allergy, and psychosomatic factors are some of the causes that have been suggested. The presence of free hydrochloric acid in the gastric juice is a prime feature of peptic ulcer. The formation of ulcers and the major symptoms of these lesions depends greatly on this factor of acidity. The very name of the lesion is a concession to the thesis that a major cause is the corrosive action of a proteolytic enzyme known to be dependent on free hydrochloric acid for its activation.

The incidence of the lesion is in itself justification for a serious consideration of the principles of therapy. A lesion that affects 10% of the total population certainly is an important one. Some observers have suggested that peptic ulcer should be treated medically except in patients with the most severe complications. Others have intimated that the lesion should be treated largely by surgical means. Somewhere between these extremes lies the truth. It is fortunate that the vast majority of patients with duodenal ulcer are able to achieve healing of the lesion and freedom from symptoms with only minor restrictions in their habits of living and eating. For some years at the Mayo Clinic, surgical treatment has been required for only about 15% of all patients in whom a diagnosis of duodenal ulcer has been made. The situation is somewhat different in gastric ulcer with surgical intervention occurring in 60 to 70% of such lesions diagnosed. A major reason for this is the ever present possibility of malignancy in gastric lesions—a problem that can be resolved most effectively by excision of the lesion. Nonetheless, a majority

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of small circumscribed gastric ulcers are benign peptic ulcers, many of which will heal promptly with adequate medical care.

Uncomplicated duodenal ulcer is properly to be considered primarily as a medical problem. With efficient application of simple well-known, readily available principles of treatment and the wholehearted cooperation of the patient in their employment, satisfactory control of the lesion will be possible in a large proportion of cases.

Many drugs and measures have been suggested in the treatment of peptic ulcer. Most have added little or nothing to the time-tried principles of treatment. Unfortunately, the public is assailed by many nostrums purporting to cure peptic ulcer. It is important for the patient who has an ulcer to realize that it is unwise to speak of medical cure of his disease; instead, he should strive to achieve control of it. He must understand that experience fails to support the idea that one medicine will be an easy answer to his problem and must realize that the principles of release from emotional tension and mental stress, use of a bland diet, avoidance of stimulants to gastric secretion, and efficient neutralization of acid give the best hope for control of his lesion. The patient must recognize that satisfactory treatment of the ulcer does not depend solely on his physician and the medicines prescribed, but that he, the patient, also must be willing to make important concessions.

All too often, the ulcer patient attempts to find release from the emotional tension that is a concomitant of his disease by over-use of alcoholic beverages, coffee, and tobacco. That alcohol and caffeine are stimulants to the production of acid is well accepted. It is only logical to exclude whatever factors tend to defeat the goal of efficient neutralization of acid. Therefore, the ulcer patient should avoid use of alcoholic and caffeine-containing beverages. Less agreement exists as to the physiologic effect of tobacco on the output of gastric juice; some investigators have reported an increase of gastric acidity, whereas others have found no change or only an occasional increase. It appears that certain patients are hypersensitive to tobacco and they will experience aggravation of their symptoms by the use or overuse of tobacco. Such persons should be enjoined to give up the habit. For the most part, ulcer patients are unwilling to discontinue the use of tobacco and some compromise must ordinarily be made in regard to this factor. Moderate smoking after meals apparently is less harmful than is smoking when the stomach is empty. Clinical experience appears to bear out the truism that an ulcer patient who is willing to forego use of alcohol and caffeine-containing beverages and stop the use of tobacco completely will stand a better chance to control the symptoms than will the patient who refuses to modify his habits in this regard or who compromises in regard to them.

Although it is considered that uncomplicated duodenal ulcer is primarily a medical disease, stubborn adherence to a medical regimen in the face of a poorly controllable ulcer is to be decried. The excellent results of surgical

treatment for duodenal ulcer in the hands of well-trained surgeons do not justify exposing a patient to the prolonged morbidity of an intractable duodenal ulcer.

Gastric ulcer presents a special problem because of the ever present hazard of gastric neoplasm and the lack of a positive clinical criterion that will assure accurate recognition of the histologic character of every gastric ulcer prior to its surgical excision. Therefore, it is wise to consider this as primarily a surgical lesion. This observation is made advisedly, recognizing the fact that a majority of gastric ulcers are benign and that many of these will heal promptly in response to supervised and adequate medical treatment.

Medical measures for duodenal and gastric ulcer must include attention to rest, alleviation of tension and anxiety, dietary modification, and the control of gastric acid by reducing its formation and neutralizing it after its production. To be successful, treatment must be adequate not only during the time of activity of the ulcer, but also during its periods of inactivity. Recognition of this principle necessitates lifetime cooperation on the part of the patient. Haphazard measures of treatment tolerated by the physician and haphazard cooperation by the patient doom to failure at the outset any medical regimen designed for the treatment of peptic ulcer, whatever its location. (Morlock, C.G., The Medical Management of Peptic Ulcer: Arch. Int. Med., 102: 594-605, October 1958)

\* \* \* \* \*

#### Corticosteroids in the Treatment of Skin Disease

The adrenal corticosteroids and related compounds have gained an unchallenged position in dermatologic therapy. These compounds, herein-after designated "corticosteroids," have securely established their worth more rapidly than any group before them and have had an unparalleled influence in the successful management of numerous diseases of the skin.

Currently, in the United States over 60 different proprietary preparations of corticosteroids are available for topical use, and scarcely a month goes by without the appearance of several more. Not only is it difficult to keep up with the various external preparations, but the corticosteroids for systemic administration are also marketed under a confusing number of names and forms.

Hydrocortisone, prednisolone, and ethamicort are the corticosteroids in most widespread use for topical dermatologic therapy today. Fludrocortisone has received somewhat limited popularity because it can be absorbed percutaneously on occasion in sufficient amounts to produce sodium retention and edema. As topical agents, the corticosteroid preparations have many desirable attributes, including (1) great efficacy in the management of

a wide variety of common dermatoses, often being rapidly effective even in small quantities; (2) ease of use and lack of stain, stink, or sting when applied to the skin; (3) no reported allergic sensitization or allergic reactions; (4) no reported untoward systemic effects attributable to percutaneous absorption (with the exception of fludrocortisone); (5) practically unlimited stability in the commonly used types of vehicles; (6) no regular increased resistance or habituation, and (7) compatibility with practically all other commonly used topical medicaments.

A Table outlines the corticosteroid preparations currently available for topical use. While this list may have been complete as the manuscript went to press, it will undoubtedly be incomplete by the time this report reaches its readers. Not only may the older corticosteroids appear in new vehicles, different packagings, various concentrations, and different combinations, but even entirely new topically active corticosteroids may be marketed. In practice, it is necessary to know a few such preparations well, including the type of vehicle in which they are incorporated, the various concentrations, the type of packaging, the presence of other active ingredients, et cetera. A second Table presents a list of the most common dermatoses which can in many cases be benefited by the topical use of the corticosteroids.

The combination of topical corticosteroids with antibiotics, such as neomycin, bacitracin, polymyxin B, oxytetracycline, et cetera, may be beneficial in controlling certain dermatoses which are secondarily infected with pyogenic organisms. Vioform, Sterosan, and Diodoquin provide antibacterial and antimycotic properties and have definite indications when used in combination with corticosteroids. When combinations of corticosteroids and antimicrobial agents are used, allergic eczematous contact dermatitis may occur to the latter. Therefore, one should be on the lookout for possible worsening of the dermatitis at the sites of treatment because such worsening may not necessarily represent an exacerbation of the original disease, but may be an allergic reaction to the incorporated antimicrobial agent. It is important to bear in mind that the clinical features of this allergic eczematous contact dermatitis may be altered by the corticosteroid and that this may make detection and diagnosis difficult.

Other combinations with tars, quinolines, and antipruritics are outlined in the first Table. The indications for the use of these corticosteroid combinations are similar to the indications for the use of the substances incorporated—for example, tar in atopic dermatitis, eczematous dermatitis, and seborrheic dermatitis, Vioform in nummular eczema, and so on.

The steroids have, thus far, proved to be among the safest of all topically applied medications. This does not apply to fludrocortisone because of the percutaneous absorption which sometimes takes place in sufficient amounts to cause fluid retention. When employing fludrocortisone, the authors generally confine its use to limited areas of skin in

adults who do not have clinical or anamnestic evidence of renal or cardiac disease. Contraindications to the topical use of steroids may include thermal burns and herpes simplex infections (certainly and especially when involving the eye). Some investigators have also considered pyodermas to be contraindications to the topical use of the corticosteroids, but the authors have not seen clear-cut worsening of bacterial skin infections resulting from the applications of these preparations. In the presence of bacterial infections superimposed on an underlying dermatitis, it is logical to use anti-septics or antibiotics separately or in combination with the topical corticosteroids.

When the corticosteroids are employed systemically in the management of dermatologic conditions, the following major factors must be taken into consideration:

1. Does the disease represent an indication for their use?
2. Are there contraindications to their use?
3. Can and will the patient remain under constant medical supervision while receiving these medicaments?

It is mandatory that the physician consider all the findings of the history and physical examination before beginning therapy. The main attention should be focused on tuberculosis, diabetes, heart disease, hypertension, renal disease, mental disturbances (institutionalization, psychiatric care), thrombotic episodes, gastrointestinal disturbances (particularly in relation to peptic ulcer), chronic focal infections, and osteoporosis, or recent fractures. As a result of the increasing knowledge concerning the systemic use of the corticosteroids, a history or presence of one or more of these conditions is no longer an obligatory contraindication to the use of a selected corticosteroid. Provided that necessary medical precautions are taken, and provided the patient can be followed carefully and observed frequently, these compounds usually can be administered even for prolonged periods without prohibitive side effects.

Topical corticosteroid therapy holds an unchallenged position of value in the management of many common skin diseases. These effective, easily used, agreeable and, to date, eminently safe steroid compounds have found widespread use in a broad spectrum of common dermatoses.

Systemic corticosteroid therapy has prolonged life—not to say saved it—for many who have other cutaneous diseases which, while not fatal, are ordinarily physically crippling and emotionally incapacitating.

Indications and contraindications for the topical and systemic administration of the corticosteroids are set forth in detail. Special problems relating to short-term and long-term systemic corticosteroid therapy are discussed. It is emphasized that the physician's constant understanding and supervision are required to manage patients receiving systemic corticosteroid therapy, for without conscientious and regular medical examinations, serious sequelae may arise from the injudicious or indiscriminate systemic

use of these potent compounds. (Sulzberger, M. B., Witten, V.H., Kopf, A. W., The Topical and Systemic Use of Corticosteroids in the Treatment of Skin Disease: Postgrad. Med., 24: 379-392, October 1958)

\* \* \* \* \*

### Encephalitis

In the United States, there are three arthropod-transmitted viral encephalitides of primary importance—western equine encephalitis, eastern equine encephalitis, and St. Louis encephalitis. In addition, there is a distinct possibility that other as yet uncharacterized or unknown types may occur. When countries other than the United States are considered, a variety of diseases must be added, including Venezuelan equine encephalitis, Japanese B encephalitis, louping-ill, and Russian spring-summer encephalitis, along with a substantial number of viruses whose specific relationship to human disease has not yet been definitely established. When considered together, therefore, sheer numbers of viruses and the diseases they cause make the arthropod-borne encephalitides a complex and somewhat formidable subject. This complexity is further compounded by the fact that, like many other insect-borne infections, the epidemiology of these encephalitides is singularly involved. Thus, in attempting to determine and understand the factors which permit the maintenance of these viruses in nature and allow their transmission to man, there must be considered not only the host-parasite relationships between man and virus, but also the relationships which exist between virus and vector and between the vector and man.

In this country, the three types of arthropod-borne encephalitis viruses produce acute inflammatory diseases of short duration involving parts of the brain, spinal cord, and meninges. The signs and symptoms of infection with arthropod-borne encephalitis run the entire gamut from a clinically inapparent infection, through a mild nonspecific syndrome of headache, fever, and malaise, to the fatal case with steady progression from headache, fever, and stiff neck up to lethargy or confusion, stupor, coma, and death. In most cases, recovery is complete, but some individuals—particularly young children—may be left with sequelae of mental retardation, convulsive seizures, spasticity, or milder evidence of neurologic damage. Mortality in apparent infections ranges from 5 to 75% and is highest in infants and the aged. No specific treatment is known for any of them.

With regard to distribution, the three infections are endemic in a number of areas. Western equine encephalitis occurs in all of the states west of the Mississippi River and extends eastward into Wisconsin and Illinois; in addition, isolated occurrences have been reported in Michigan, Kentucky, Tennessee, Alabama, North Carolina, New Jersey, and Rhode Island. St. Louis encephalitis has a similar distribution west of the

Mississippi River with important extensions eastward into Illinois, Indiana, Ohio, Kentucky, and Tennessee. Eastern equine encephalitis—the rarest of the three—occurs principally along the Atlantic and Gulf States from Massachusetts to Texas with isolated occurrences reported in Tennessee, Wisconsin, Michigan, Kansas, and Missouri. Taking the three types together, a distribution map would involve essentially the entire country with the exception of northern New England. Even in those states, it is possible that virus activity might be demonstrated in reservoir hosts. In 1956 alone, these virus infections were demonstrated conclusively in 25 states in man and horses, in their natural reservoir in wild birds, and/or in the various species of mosquitoes which transmit them; in all but eight or nine of the remaining states, there was strong presumptive evidence of the presence of at least one of these viruses.

Even with the most liberal interpretation of available data, it is obvious that the cases of arthropod-borne encephalitis cannot compare numerically with many of the other communicable diseases. From the standpoint of health departments in the areas where they occur, these three infections have special significance. The very nature of the disease with its greatest severity in children, the somewhat frightening terminology of "sleeping sickness" commonly employed by the press, the often explosive nature of an outbreak or epidemic, and the general lack of knowledge in the population at large concerning these infections—all result in public clamor that "something must be done" when cases occur.

The arthropod-borne encephalitides in this country are of sufficient public health importance to merit serious consideration. Further, there is every reason to believe that—provided with the necessary epidemiological information—effective and practical control methods can be developed for these diseases as they have been for malaria, typhus, and other arthropod-transmitted infections. (A. W. Donaldson, ScD., Arthropod-Borne Encephalitis in the U. S. A., Am. J. Pub. Health, 48: 1307-1314, October 1958)

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#### Diagnostic Significance of Muscle Biopsy

Skeletal muscle may be the site of lesions in many disorders. Involvement of the muscle may be suggested by the presence of such symptoms and signs as pain, weakness, tenderness, atrophy or wasting, and hypertrophy, but may occur in the absence of obvious clinical manifestations and can then be established only by the examination of muscle tissue obtained at biopsy or autopsy. The pathologic abnormalities seen may be diagnostic of the disorder or may be nonspecific.

Great emphasis has been placed on the diagnostic value of the microscopic study of muscle tissue. During the last several years, there have

been references to its value in polyarteritis, rheumatoid arthritis, dermatomyositis, and polymyositis, disseminated lupus erythematosus, scleroderma, sarcoidosis, and myasthenia gravis; and an excellent general survey of muscle pathology has appeared. Nevertheless, there remains some doubt as to the diagnostic specificity of many of the changes seen in muscle. For example, arteritis of various sorts is seen in many diseases other than polyarteritis, and inflammation and muscle degeneration in diseases other than dermatomyositis.

Tissue removed at muscle biopsy normally includes muscle fibers, supporting connective tissue stroma, and the blood vessels contained in that stroma. There are only a limited number of ways that each can respond to injury. Muscle fibers can show degenerative changes for example, in response to a large number of different stimuli, including even excessive handling during the biopsy procedure. For this reason, the authors classified their findings in two ways. First, the general pathologic changes seen in muscle during this study; following this, the pathologic condition of the muscle in specific medical disorders. The general changes can further be subdivided into vascular, interstitial, connective tissue and muscle fiber abnormalities.

The study of muscle pathology may be of relatively little help in clinical diagnosis in most medical disorders. In this study, only in some patients with trichinosis, sarcoidosis, and polyarteritis, were pathologic changes seen in muscle which were sufficiently specific for diagnostic purposes. In other patients, the changes were either common to many diseases and, therefore, nondiagnostic, or no abnormalities were noted.

A retrospective evaluation of the random skeletal muscle biopsy at the Columbia-Presbyterian Medical Center, 1946 - 1956, is reported. Changes seen on examination of muscle tissue were of value in diagnosis in some patients with sarcoidosis, polyarteritis, and trichinosis. The characteristic lesion in the muscle in sarcoidosis was the epitheloid cell granuloma with giant cells, such as is found in other tissues in this disorder. This lesion was found in muscle in slightly more than 50% of patients with sarcoidosis. In 37% of patients with polyarteritis, acute arteritis with necrosis of the vessel wall, inflammatory cell infiltration with or without granulomas, was found in the muscle. In only 3 of 15 patients with trichinosis were trichinae seen in the muscle specimen obtained at biopsy.

In those mentioned, and in other medical disorders, muscle fiber degeneration associated with inflammatory changes was often encountered. Although such lesions occurred with greater frequency and perhaps with greater severity in the muscles of patients with dermatomyositis and polymyositis, they were found in such a wide variety of disorders that they could not be considered to have diagnostic specificity. (Wallace, S. L., Lattes, R., Ragan, C., Diagnostic Significance of the Muscle Biopsy: Am. J. Med., XXV: 600-608, October 1958)

Uncommon Roentgen Patterns

The common roentgen features of intrathoracic sarcoidosis have been adequately described and clearly depicted in the literature. Numerous reports illustrate the variegated manifestations of the disease: the lymph node enlargement, disseminated miliary densities, localized infiltrates, and the fibrotic changes, alone or in combination.

However, not all cases reveal these more or less typical findings. The present report deals with two interesting but less familiar roentgen patterns of pulmonary sarcoidosis which may, at times, bring this disease to mind—the multinodular and the multicystic.

The multinodular pattern of sarcoidosis has received little mention in the literature, only a few cases having been recorded. The author had opportunity of studying the roentgenograms in five cases including the two reported by McCord and Hyman. In four instances, a roentgen diagnosis of malignant pulmonary metastases was originally made. However, the mild clinical symptoms and the continued well-being of the patients led to further study and, ultimately, microscopic evidence of sarcoid was obtained, twice from the lung and twice from a peripheral lymph node. In the fifth case, sarcoid was suspected clinically and roentgenologically; the diagnosis was confirmed by scalene lymph node biopsy. Four of the five patients were young Negroes and the fifth was a Negress, age 26. All were mildly ill with general symptoms, such as fever, malaise, night sweats, and weight loss; and respiratory symptoms, such as cough, dyspnea, and expectoration. All but one showed peripheral lymph node enlargement of slight to moderate degree and two showed elevation of the serum globulin and serum calcium. No other clinical evidence of systemic sarcoidosis was apparent.

In each case, the chest roentgenogram revealed changes far out of proportion to the mild clinical manifestations. There were numerous round or oval lesions, 5 to 40 mm. in diameter, widely distributed in the lungs. In four cases, the nodules appeared to be more numerous in the central zones where they tended to be confluent. The individual nodules in these 4 cases presented a hazy or fluffy outline, the "soft" margin sometimes appearing as a halo around the central density. The confluence of the nodules and their lack of sharp borders did not closely simulate the common type of metastases, but the resemblance to the "halo" nodules of chorionepithelioma, also seen occasionally with other metastatic tumors, was striking. The fifth case showed scattered sharply outlined nodules varying from about 5 to 15 mm. in diameter and in no way different from the appearance of the garden variety of pulmonary metastases.

In 3 cases, the superior mediastinum appeared widened, presumably due to lymph node enlargement. In only one was hilar lymph node enlargement apparent, but in 3 others, the overlying pulmonary lesions obscured the hilar areas.

The multinodular roentgen pattern described in the report cannot be considered diagnostic of sarcoidosis. This is a rare manifestation of this disease and perhaps would more often result from tumor metastases of pulmonary lymphoma. Multiple histoplasmoses, the nodular form of tuberculosis, and multiple benign tumors (e.g., hamartomas) must also be considered in differential diagnosis, but in these conditions, the nodules are fewer and sharper in outline; often some of them contain calcium.

Certain features encountered in the present group of cases should provide the clue to the correct diagnosis. These include the mild clinical symptoms and the continued well-being of the patients; the presence in other body systems of stigmata consistent with sarcoidosis, especially lymphadenopathy; the apparent predilection for young Negroes; the fluffy margins of the pulmonary nodules and their tendency to become confluent; and the stationary or even regressive course shown roentgenographically.

The multicystic pattern of sarcoidosis is probably a complication of the irreversible fibrotic stage of the disease. It is not infrequently encountered at the autopsy table in patients who have died of sarcoidosis, but has seldom been emphasized as a prominent or predominant roentgen manifestation of the disease.

The author's experience with the multicystic pattern of sarcoidosis dates back about 10 years and is based on 9 proved cases. Six were seen at the Cincinnati General Hospital and represent 21% of the 28 proved cases of sarcoid at this institution in which chest roentgenograms were available. The remaining three cases came from other institutions in the area.

All of the 6 cases from the General Hospital were Negro (Negroes account for about 50% of the hospital admissions), but the 3 outside cases were white. There were 5 women and 4 men in the group. The ages ranged from 29 to 63 years with an average of 38 years. Comparable figures for the control group of 22 cases of sarcoid from the General Hospital who did not show the multicystic pattern were: 22 Negro, 0 white; 18 women, 4 men; age range, 19 to 49 with an average of 31 years—7 years less than that of the multicystic group.

On the initial roentgenogram, multicystic lesions were the predominant feature in only 1 case, although they were present to some degree in several others. In the remaining 8, extensive pulmonary infiltrate was apparent, fibrotic in nature in 6 and miliary in 2 cases. In 2 cases, 1 with fibrosis and 1 with miliary densities, the involvement was limited to one lung. The unilateral miliary lesions exemplified an exceedingly rare distribution of this form of sarcoidosis. Mediastinal and/or hilar enlargement was evident on the first film in 7 cases and appeared later in 1. Spontaneous pneumothorax occurred terminally in 1 case.

In the differential diagnosis, any condition which causes widespread pulmonary fibrosis which, in turn, results in bullous emphysema or cystic bronchiectasis, must receive consideration. Many diseases fall into this

category, including tuberculosis, histoplasmosis, diffuse interstitial fibrosis of Hamman and Rich, scleroderma, bronchiectasis, progressive bullous emphysema or "vanishing lung," pneumoconiosis, and the later stages of chronic bronchial asthma. These conditions often closely simulate multicystic sarcoidosis roentgenographically as well as clinically. However, the enlarged tracheobronchial nodes, earlier chest roentgenograms showing the more typical appearance of sarcoid, and the presence of other clinical and laboratory evidence consistent with sarcoidosis suggested the correct diagnosis in a number of the cases in the present series.

The seriousness of the multicystic form of pulmonary sarcoidosis is evident when it is pointed out that 5 of the 9 cases have died and that 2 others were doing poorly when last seen.

The sequential roentgenograms appear to substantiate the viewpoint that the cystic changes result from pulmonary fibrosis. While it is realized that the roentgen recognition of fibrosis is not always reliable, the criteria used in the present cases seem adequate. These included strand-like densities, persistence of the shadows for periods in excess of a year, and retraction of fissures, hila, and mediastinal structures.

It is realized that there is no microscopic picture which is pathognomonic for the diagnosis of sarcoid. However, the presence of compatible clinical and roentgen findings, when added to the demonstration of non-caseating granulomas, leaves little doubt that these patients suffered from sarcoidosis. Also, it is apparent that the multicystic pattern represents a late manifestation of this disease. (Felson, B., Uncommon Roentgen Patterns of Pulmonary Sarcoidosis: *Dis. Chest*, XXXIV: 357-365, October 1958)

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#### Penetrating Keratoplasty

Transplantation of the cornea is undoubtedly one of the most fascinating subjects in modern ophthalmology. During the last 19 years, the author has had the opportunity of doing 148 of these grafts, principally at the Massachusetts Eye and Ear Infirmary and St. John's Hospital, Lowell, Mass. The author emphasizes points on transplantation which experience indicates to be of more than ordinary interest or importance. A statistical analysis of 100 consecutive transplants, 1944 to 1954, is included.

Transplants are classified in two ways, by surface area and by depth. According to area, they are total if the entire width of the cornea is used, and circumscribed or partial, if only a window is taken from the cornea. According to depth, they are lamellar when only the top layers of lamellas are replaced and penetrating when the full thickness of the cornea is transplanted. Thus, one recognizes four types: total and partial lamellar, and total and partial penetrating keratoplasty. Until a few years ago, only the

partial penetrating was considered of value; but lamellar grafts also are now widely used.

The first key to success is the proper selection of cases. Favorable cases are those in which the eye is normal except for the cornea; the leucoma, or scar, is not dense or vascular; and there are areas of clear or slightly scarred cornea surrounding the graft to furnish it nutrition. Especially unfavorable cases are those with dense scarring of the entire cornea, vascularized pannus from old trachoma or severe chemical burns, and edema of the cornea as in Fuch's dystrophy. In the author's experience, the "most favorable cases" have been the following groups in the order listed: (1) small central scars from any cause, (2) keratoconus, (3) Groenouw's familial dystrophy and lattice keratitis, (4) diffuse thin scarring as from old phlyctenular keratitis, and (5) old interstitial keratitis with irregular moderate scarring.

The location for the new graft should be picked carefully. It should be in an area that leaves as much clear cornea for its border as possible. This is of great benefit to the nutrition of the graft; and, in fact, the amount of healthy corneal tissue at the graft margin is probably the most important single factor in determining the ultimate success of the graft.

The graft should also be located so that it will lie within the pupillary area or the opening formed by the pupil plus the preliminary iridectomy in order to lessen the chance of anterior synechias.

In keratoconus cases, it is desirable that the entire thin part of the cone should be removed so that the edge of the graft will be in contact with host cornea of at least 60% normal thickness. This generally calls for a graft at least 6 mm. in diameter with the center often slightly down and to the nasal side.

The size of graft preferred in ordinary cases varies with the surgeon and with the size and shape of the corneal scar, but most of the author's cases were from 4.5 to 6 mm. with the great majority being 5 mm. in width. The 5-mm. graft is also most widely used by other surgeons. The smaller the grafts, the less the chance of dislocation and anterior synechias, so before the advent of direct sutures, a 4.5 mm. graft was desirable for patients whose postoperative behavior was distrusted, or for eyes in which the pupils could not be dilated.

If a cataract is present, the graft should be done first and the cataract removed about 4 months later as the chance of a successful graft in aphakic cases is very slight. Following the transplant, a cataract extraction is no more difficult than on a normal patient. Former glaucoma cases must be under complete control without miotics. Nystagmus is not necessarily a contraindication.

During the 19 years included in this 148-case series, corneal transplantation has grown from a speculative procedure to a successful and well-established ophthalmic operation. Due to continuous improvements in therapy,

keratoplasty is a far more successful procedure at the present time than it was even 5 years ago. Among recent improvements stressed are:

1. Preoperative preparation for grafting by elimination of blood vessels by radiation and, in extreme cases, by superficial keratectomy and conjunctival recession.
2. Improvements in fixation of the graft. Detailed descriptions are given of two original track suture techniques and of several new instruments, including a plastic turret style graft holder to facilitate suturing of the graft.
3. Prevention of anterior synechias, principally by the use of air in the anterior chamber and, to a lesser extent, by improvements in graft suturing.
4. Use of steroids topically and orally for combating edema and inflammation with its attendant complications.
5. Prevention of vascularization in the new graft by reduction of inflammation and by use of beta radiation.

Of the complications encountered, glaucoma was one of the more frequent, being present at some time during convalescence in 33% of the cases.

Anterior synechias were extremely common in the early cases, but in the more recent 100-case series, they occurred in only 23% of cases. Edema of the cornea and proliferation of connective tissue on the back of the graft were also major complications. Infection and traumatic cataract each occurred once during the entire 148-case series.

Long postoperative follow-up (19 years in some cases) suggests that progressive dystrophies of the cornea eventually recur in the new cornea at the same rate as in the original cornea. Because the time required for reappearance is usually many years, the probability of recurrence is not a contraindication to grafting.

Results of the entire 19-year series of 148 cases were 63.5% "improved." Recent results are much better than those of the 1930's and, for the sake of current statistics, analysis is presented of 100 consecutive grafts (91 primary and 9 regrafts) done in recent years. In this series, running from 1944 to 1954, results were 69% "improved," 19% "unchanged," and 12% "worse."

In this latter series, results in "most favorable cases" (keratoconus, nodular dystrophy, and lattice keratitis) were excellent, with 32 out of 37 being improved (86.5%). By etiologic groups, results were: keratoconus, 100%; nodular dystrophy and lattice keratitis, 79%; interstitial keratitis, 63%; disciform and dendritic keratitis, 69%; leucomas from pyogenic ulcers, 45%; chemical burns, 60%; edema of cornea (similar to, but not true Fuch's dystrophy), zero percent; regrafts (miscellaneous), 33%.

Because the results in this 100-case series are better than those of the previous 7 years, and results during the past few years have been better than

those in the first part of the series, it is reasonable to expect that transplant statistics will continue to grow more favorable for many years to come. (Leahy, B.D., Penetrating Keratoplasty - Observations Based on a Series of 148 Cases with Special Emphasis on Techniques of Graft Fixation: Am. J. Ophth., 46: 541-581, October 1958)

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### Myxomatous Tumors of the Jaws

Because myxomas and fibromyxomas of the jaw are rare, description of these tumors in the dental literature usually has been in the form of individual case reports. This article reports on 26 lesions of this type seen at the Mayo Clinic and gives special attention to the correlation of histologic and clinical characteristics.

Thoma, discussing etiology and classification of myxomatous lesions of the jaw, grouped these tumors into osteogenic and odontogenic types. The more common odontogenic tumors, he stated, were almost always benign and the osteogenic tumors were most often malignant, like myxomatous lesions in other bones.

Among reported cases, males and females were affected with almost equal frequency. Seldom was the patient younger than 10 years or older than 50 years; almost 67% of the patients were between 10 and 29 years of age.

Almost two-thirds of the lesions described in the literature were in the mandible. Within the mandible, the angle of the jaw, the ramus, and the adjacent molar region were most commonly affected, but some tumors extended anteriorly. A few affected primarily the anterior portion, but bilateral tumors were rare. Within the maxilla, the zygomatic process and alveolar bone bearing the molar and premolar teeth were affected most often. Frequently, the sinus was involved, especially by larger tumors. Tumors of the anterior maxilla were less common.

The sign most frequently reported was a slowly progressive swelling and facial deformity, usually painless. The teeth in the affected region often were malposed, but more frequently they had been extracted in an attempt at treatment. Some teeth had been loosened because of destruction of the supporting bone. The mucosa was normal except for occasional ulceration secondary to biopsy or dental extraction. These signs and symptoms had been noted for periods varying from 1 week to 8 years, usually from 1 to 3 years, before treatment was begun.

The typical roentgenologic appearance of the tumor was described as a multilocular radiolucent area with well-defined, sclerotic margins. A few lesions were unilocular. On extension of the lesion into the alveolar bone, the margin sometimes became scalloped between the roots of the teeth.

Although some authors stated that the tumor showed no trabeculation, Sonesson used the presence of gracile straight trabeculae to help distinguish this tumor from cysts and ameloblastomas as well as from fibromas and even fibrous dysplasia which are extremely difficult to differentiate by roentgenologic means.

The mandible bearing a tumor often was expanded; the cortex was sclerotic and usually intact. In the maxilla, the tumor invaded not only the bone, but the antrum as well, appearing as a large rounded mass of soft tissue on the anteroposterior or Waters' views. Occasionally, the antral walls were destroyed by the tumor.

Invasion of soft tissue is more characteristic of ameloblastomas than of myxomas. The tumors were reported to vary from 1 to 10 cm. in diameter. Most authors agreed that cyst, fibroma, ameloblastoma, giant-cell reparative granuloma, and fibrous dysplasia must be included in the differential diagnosis because of their similar roentgenologic appearance. Hovnanian believed that the diagnosis of sarcoma must be entertained even though the lesion appears roentgenologically benign.

Myxomas and fibromyxomas of the jaw were found to be persistent lesions and most difficult to eradicate; however, like the ameloblastomas, they were benign. Stout declared that metastasis of myxomas never has been reported except in tumors of the heart; other authors likewise stated that metastasis does not occur. Most authors agreed that sarcomatous change eventuates rarely, if ever.

The prognosis for the benign lesions is excellent in the sense that the patient's life is not jeopardized and no malignant changes in bony lesions of this type have been demonstrated. However, even the benign lesions are difficult to eradicate and, unless completely removed, recur rapidly. None of the patients in the present series is known to have died as a result of the tumor.

Because of the extensive local involvement and the tendency to recur, the tumor must be vigorously treated. One surgeon expressed the opinion that block excision within the continuity of the bone, when feasible, was probably the best form of treatment for these tumors; both he and the roentgenologist who worked with him decided that radiation was of no value in treating myxomas and fibromyxomas.

The judgment of the authors, however, is that resection is indicated as a first measure only in cases of massive lesion. For recurrent tumors, more radical treatment may be necessary. Also, agreement was reached that irradiation is probably of no value in the treatment of these tumors and it is now known that irradiation of benign tumors of bone is potentially hazardous. (Zimmerman, D. C., D. D. S., Dahlin, D. C., M. D., Myxomatous Tumors of the Jaws: *Oral Surg.*, 11: 1069-1079, October 1958)

Navy Problems in Cold Weather Medicine

(The following article reviews some of the cold weather medical problems as they apply to the Navy. Special emphasis is placed on physiologic and psychologic adjustments, nutrition, clothing, shelter, environmental sanitation, first aid and evacuation of the injured. It also presents Navy research that has been done in some of these areas. Due to its length, this review prepared by CDR D. Minard MC USN, will be presented in two consecutive issues of the Medical News Letter. Clinical aspects of cold injury including frostbite, immersion foot, and immersion hypothermia have been described in previous issues of this publication.)

Navy training and logistics operations in the Arctic and Antarctic have demonstrated the capability of naval surface vessels and aircraft carriers to conduct operations at high latitudes in sea areas adjacent to the polar ice packs. The nuclear-powered submarine USS NAUTILUS crossed the North Pole beneath the ice pack itself.

Medical officers of the Navy are responsible for maintaining and promoting health and efficient performance of Navy and Marine Corps personnel exposed to cold weather while engaged in duties aboard ship, in amphibious landings, and in combat operations on shore. Special problems in the cold are encountered by Navy fliers and frogmen.

Physiologic Adjustments to Cold

Being a homeothermic animal, man depends on a uniform internal thermal environment for optimum function of vital tissues. When he is exposed to cold, reflex autonomic adjustments divert warm blood away from the skin, allowing the skin to cool and thus reducing heat loss by radiation and convection to the cold environment. If heat loss continues to exceed heat production shivering ensues, a process which can elevate metabolic heat production as much as five times the basal rate.

Thus, by first allowing its shell to cool and second by elevating metabolic heat production through shivering, the body preserves uniformity of its core temperature. In extreme cold or with inadequate thermal insulation, heat loss will continue to exceed heat production despite these adjustments; core temperature, too, will begin to fall. Unless the drain of heat from the body is interrupted, fatal hypothermia is inevitable.

Individuals differ in their tolerance to cold, not only in terms of the metabolic cost of maintaining core temperature, but also in the ability to maintain warm, functional hands. Body composition which affects the insulating value of tissues and body size and configuration which determines the surface to volume ratio can explain some of these differences. Less is known of the role played by individual differences in autonomic, endocrine, and metabolic responses to cold.

Through acclimatization, it now appears, that the same individual can acquire increased tolerance to the local and general effects of cold. Although numerous studies have produced ample evidence of true cold adaptation in various animal species as indicated by changes in circulation, endocrine activity, and in intermediary metabolism, the physiologic mechanisms of cold acclimatization in man are still poorly understood.

If it were possible to identify the man inherently tolerant to cold, and also the one who can acquire high cold tolerance, it might be possible to preselect men for special cold weather assignments and to screen out those apt to perform poorly in the cold, thereby improving the efficiency of cold weather operations.

#### Psychologic Adjustments to Cold

Achieving a healthy mental attitude toward living at high latitudes is more of a problem for the man based on shore than for his comrade aboard ship. The latter remains in a familiar environment modified only little by climatic cold and ice. He continues to share the responsibilities of operating the ship with his crewmates and continues doing a familiar job. Hence, there is little threat to his security.

The man on shore for the first time in the Arctic is in a strange and potentially hostile environment which may appear to threaten his very existence. Much of his time is spent merely keeping himself warm and fed. He becomes preoccupied with his own problems and may withdraw from friends and associates. Anxiety reactions and personality disturbances commonly follow, manifesting themselves as functional disorders, moodiness, irritability, insomnia, overeating, and perhaps proneness to accidents. Under emotional and physiologic stress imposed by this environment, inapparent psychosis may become manifest.

In preventing psychologic maladjustment and psychiatric casualties in personnel on cold weather duties, the medical officer should observe the following principles: Prior to assignment to cold weather duty, men must be motivated to accept willingly such duty through explanation and assurance of the importance of their tasks and by stimulating their interest for new experiences in a totally new environment; a psychiatric examination to screen out those apt to become psychiatric casualties is a necessary part of the medical examination for such assignment; thorough indoctrination in methods of living in the new environment prior to arrival there will do much to allay fear based on ignorance; finally, competent leadership during the tour of duty will promote in the man confidence in himself and healthy attitudes toward his fellows in work and in group recreation.

#### Nutrition

With rations now available to shipboard and land based personnel in Arctic and Antarctic areas, deficiency diseases are essentially nonexistent.

In special situations, such as may exist in combat or on the trail where men may be required to subsist for periods on E Rations, supplements of Vitamin C may be added as a precautionary measure against subclinical scurvy.

Although there is some dispute on the point of caloric requirements, the prevailing opinion is that the need for calories is elevated in cold environments. Ration allowances are, therefore, increased 15%. It is not known whether the added calories are needed because of increased heat loss to the cold environment, reduced efficiency of muscular work, stimulation of metabolism by the cold, or other factors. There does seem to be increased appetite and men commonly put on weight in cold weather zones, indicating that the increased intake of calories may often exceed the actual energy output.

Other nutritional problems which need further study in cold weather are the optimal frequency of meals, composition of the diet with special references to the amount and quality of fat, and the use of high protein intake to stimulate metabolic heat production through its specific dynamic action.

#### Clothing

The ability of the Eskimo to live in the Arctic depends more on his ingenuity in keeping a warm environment near his skin with clothing and shelter rather than upon inherited or acquired resistance to the Arctic climate.

The problem of Arctic clothing is basically not so much that of providing sufficient insulation as that of devising means of varying its insulating capacity to meet changing needs. Clothing which provides adequate protection to an active man may be wholly inadequate for a man at rest or asleep. Conversely, men doing heavy work in cold weather clothing tend to sweat. This has two serious results; First, the moistened clothing loses its insulating qualities, and second, moisture trapped in the fabric continues to evaporate after work is over resulting in postexercise chill. Up to now, the solution to this problem has been to remove or add layers of clothing as dictated by weather and activity.

A promising new development in clothing technology is the Cold Bar uniform consisting of a single layer of expanded plastic material which possesses excellent insulating qualities. Insulation is adjusted by opening or closing vents. Lack of mechanical strength has thus far prevented its extensive use in the field.

The vapor barrier combat boot, when properly used, can eliminate most cases of frostbite of the feet. Improperly used, the boot creates new problems as a result of waterlogging the skin which leads to maceration, trauma, and infection. Conventional types of footwear are still widely used in the Arctic.

The problem of protecting the hands from cold without serious interference with manual dexterity is still largely unsolved. Engineering redesign of the manual controls of weapons, vehicles, and electronic instruments so as to permit manipulation by gloved and mittenized hands may possibly be the most promising approach.

Cold weather clothing for use on weather decks of ships and in amphibious operations must be relatively impervious to spray and other outside sources of wetness. In addition, there is a need for an immersion suit impermeable to water which can be quickly donned in abandoning ship, and also one which can protect assault troops in landing craft from accidental immersion in icy water during landing operations. It is axiomatic that in ship-to-shore movements in the Arctic, troops must be "dry landed." This requires special techniques in loading men and their equipment aboard landing craft. Amphibious tracked vehicles and LST's have demonstrated their value in landing troops in dry condition. Boat teams for rescuing and treating cases of immersion and shore facilities for exchanging wet for dry clothing are a necessity in such operations.

#### Shelter

Modern Navy vessels at sea constantly burn large quantities of fuel for propulsion and for generating electricity. Even in Arctic waters, there is heat to spare. Men can live and work below decks in comparative comfort despite minor annoyance from low relative humidity and drafts.

On the barren shore of the polar regions, however, fuel is a scarce commodity. To be used economically for keeping bodies warm, fuel must be burned within shelters in order to hold in the heat and keep out the cold. Various temporary and semipermanent prefabricated structures with insulated walls and floors have been devised for use by land forces. Typical of these is the Jamesway hut.

Recently, experimental Arctic shelters of efficient design have been fabricated from light weight rigid plastic material. Combining strength with excellent insulating qualities, such shelters will doubtless replace more familiar designs in time.

To prevent carbon monoxide poisoning, special care is required in operating heaters within shelters. Automatic CO detectors which signal the presence of dangerous concentrations of this deadly gas are essential items of equipment. (Thermal Stress Branch, OccMedDispDiv, BuMed)

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#### Industrial Injuries of the Foot

Most of the complex injuries involving loss of tissue are seen at some time during their course by the plastic surgeon. In California, during 1956,

the Department of Industrial Relations reported approximately 23,000 injuries involving the feet. Figures representing the extent of the disability involved are not available, but could be expected to be staggering because loss of time from work in this type of case is notoriously prolonged.

Surgeons are inclined to study and classify such cases according to the objective observations when the patient is first seen. This may be immediately or many months after the injury and efforts are then directed towards salvaging what can be salvaged and replacing that which is lost to the best of their ability according to the general principles of reconstructive surgery. Their objective is a specialized one—to obtain healing and restore the foot as closely as possible to the normal from a purely surgical standpoint. Unfortunately, when the patient ultimately limps out of the hospital, his foot healed, the surgeon's enthusiasm is apt to drop off sharply and he is inclined to divorce himself from further responsibility or active participation in the case, relying on the physiotherapist to carry on. The plastic surgeon must not confine his interest to surgery alone; the much broader field of rehabilitation—which has been defined as a continuous therapeutic process that terminates only with recovery or successful reinstatement in some useful and economic occupation—is also his concern.

The rehabilitation of each patient should be under the direct guidance and supervision of the surgeon who has had the opportunity of close association and study during the reconstructive phase of treatment and, therefore, is in a position to know best the patient and his problems. The help and advice of specialists in this field is essential and invaluable, but indiscriminate physiotherapy can produce harmful results.

When medical science has done its best and the patient has been dismissed from further treatment, in many cases the actual objective—reinstatement of the patient in some useful and rewarding occupation—has still not been achieved. An essential factor is missing, the coordination and cooperation between the medical profession and the employer. However, there is a growing recognition of the value of the handicapped worker in industry whether the disability be temporary or permanent. All doubt has been removed that therapy can be combined with productivity. (Steiss, C. F., Industrial Injuries of the Foot: J. Internat. Coll. Surgeons, 30: 266-273, August 1958) (OccMedDispDiv, BuMed)

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#### Change of Address

Please forward requests for change of address for the News Letter to: Commanding Officer, U. S. Naval Medical School, National Naval Medical Center, Bethesda 14, Md., giving full name, rank, corps, and old and new addresses.

## HONORS

The Surgeon General, Rear Admiral B. W. Hogan MC USN, has been awarded the "Cruz Peruana al Merito Naval, en el grado de Gran Oficial Distintivo Blanco" (The Peruvian Cross of Merit) by the President of the Republic of Peru and the Peruvian Navy. The decoration was presented to Admiral Hogan through Rear Admiral Luis Edgardo Llosa, Naval Attaché, Embassy of Peru, Washington, D. C., on October 8, 1958, in connection with the celebration of Peruvian Navy Day. The basis for this high award was in recognition of the assistance which the U. S. Navy Medical Department has given to the Peruvian Naval Medical Department. (TIO, BuMed)

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## Applications for MSC Training

Information concerning the Medical Service Corps training program was promulgated in BuMed Instruction 1520.12 of 10 March 1958. Since that time the Medical News Letter has announced modifications in training requirements and deadline dates for receipt of applications in the Bureau of Medicine and Surgery.

It is planned to issue a revision of BuMed Instruction 1520.12 (particularly the enclosure thereto listing current fiscal year requirements) during the month of March 1959. In order to achieve maximum effectiveness from the limited resources planned for fiscal year 1960, more time will be necessary for processing applications for full-time training to commence on and after 1 July 1959. Accordingly, it is urged that all applications for full-time training to commence during the period 1 July 1959 through 30 June 1960 be forwarded in sufficient time to arrive in this Bureau not later than 1 Mar 1959.

All requests received from eligible Medical Service Corps officers will be considered. Selections will be made on a competitive basis to meet service requirements in such specialties as are considered appropriate in the over all Bureau responsibility for training MSC personnel.

NOTES: 1. For fiscal year 1960, training requirements are expected to exist in the same programs and at the same levels as in fiscal year 1959.

2. Convening dates for programs indicated in enclosure (1) to BuMed Instruction 1520.12 will be approximately the same months and dates in fiscal year 1960.

3. Applications are particularly invited from officers of the Supply and Administration Section interested in attending the Junior Course, Marine Corps Educational Center, Quantico, Va., (September 1959) and the Navy Management School, Naval Postgraduate School, Monterey, Calif., (August 1959) (ProfDiv, BuMed)

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Steps Recommended to Curb Staphylococcal  
Infections in Hospitals.

On the basis of findings and recommendations of the National Conference on Staphylococcal Disease held recently in Atlanta, Ga., the following measures are proposed by the Public Health Service to prevent and control hospital outbreaks:

1. Establish infectious control committees in all hospitals.
2. Employ an "infection log" for entering and classification.
3. Screen staff personnel who have boils or who are carriers.
4. Exercise discrimination in use of antibiotics.
5. Store cultures from staph infections.
6. Isolate infectious patients.
7. Take special precautions in nurseries for newborn.
8. Stress training of personnel intensively and continuously.
9. Strengthen laboratory services and expand research.

(ProfDiv, BuMed)

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From the Note Book

1. In ceremonies at the National Naval Medical Center, Bethesda, Md., October 23, 1958, the Surgeon General of the Navy, Rear Admiral B. W. Hogan, accepted for the Navy an oil painting of Dr. Edward Robinson Squibb, Passed Assistant Surgeon in the Navy during the decade, 1847-1857, and founder of the pharmaceutical firm bearing his name. Presentation of the painting was made by George S. Squibb, great-grandson of Dr. Squibb, in connection with the celebration of the firm's 100th anniversary. (TIO, BuMed)
2. Captain C. T. Pridgeon DC USN, on duty at the U. S. Naval Support Activities, London, England, recently presented an essay, "The Role of the General Practitioner in our Periodontal Problem," before members of the Essex Branch of the British Dental Association at their annual meeting held in Chelmsford, England. (TIO, BuMed)
3. Commander G. H. Rovelstad DC USN under instruction in Dental Research at Northwestern University, Chicago, Ill., recently presented a paper on "Characteristics of Saliva of Caries Free Young Male Adults," before the Chicago Chapter of the International Association for Dental Research held at the Institute of Medicine in Chicago. (TIO, BuMed)

4. The problem of maintaining adequate oral hygiene in handicapped children is often the most serious that the dentist has to contend with in treating these children. A study of the efficacy of a chlorpactin mouthwash as an adjunct to oral hygiene was made in a group of handicapped children. The patients who used chlorpactin mouthwash showed a marked improvement in oral hygiene. (Oral Surg., October 1958; E. J. Weisman, D. D. S.)
5. This review indicates, by means of specific examples, how some of the physiological changes associated with sleep may affect the pathologic physiology of some diseases. (Arch. Int. Med., October 1958; E. D. Robin, M. D.)
6. This study concerns the patient admitted to the hospital for a specific surgical procedure. The purpose was to evaluate the patient's psychological status, his feelings about hospitalization, anesthetic procedures, and the surgical experience in relation to his course in the hospital and any postoperative behavioral reactions. (Am. J. Surg., November 1958; H. H. Corman, M. D., et al.)
7. Vision in the animal world, the story of how animals came to see, what they see, and what they make of this world is the subject of the Lister Oration delivered by Sir Stewart Duke-Elder before the Royal College of Surgeons. (Am. J. Ophth., October 1958)
8. By means of careful clinical evaluation, it is possible to determine the capacity of cardiac patients for work. Availability of engineering analysis of various jobs, expressed in the same capacities, permits proper placement by matching the patients' capacities with the demands of the job. Employees with partially disabling heart disease may continue to work effectively with proper treatment. (Postgrad. Med., October 1958; N. K. Weaver)
9. This article presents data helping to define changes in the differential white cell count acceptable for the diagnosis of infectious mononucleosis. The evaluation of a positive heterophil test in the absence of diagnostic hematologic findings is discussed. (Ann. Int. Med., October 1958; C. E. Bender, M. D.)
10. This article evaluates the result of surgical closure of the various types of atrial septal defect by several techniques listed and defines indications and contraindications for closure. (Dis. Chest, October 1958; S. A. Kieffer)
11. This article presents the pertinent roentgenographic features of the various lesions of the renal papillae and of the major and minor calyces. (Am. J. Roentgenol., October 1958; B. S. Abeshouse, M. D., J. O. Salik, M. D.)

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Recent Research ReportsNaval Dental Research Facility, NTC, Bainbridge, Md.

1. Survey of Dental Health. IV. Relation of Frequency and Regularity of Dental Visits. NM 75 01 26.04, 28 August 1958.
2. Survey of Dental Health. V. Relation of the Age of the Recruit. NM 75 01 26.04, 15 September 1958.
3. Survey of Dental Health. VI. Relation of Place of Birth. NM 75 01 26.04, 30 September 1958.
4. Survey of Dental Health. VII. Relationship of the Score on the General Classification Test. NM 75 01 26.04, 15 October 1958.
5. Survey of Dental Health of the Naval Recruit. VIII. Relation of Formal Education. NM 75 01 26.04, 15 October 1958.

Naval Medical Research Institute, NNMC, Bethesda, Md.

1. Thermodynamics of Muscle. NM 03 02 00.01.02, 16 May 1958.
2. Design of a Miniature Radio Transmitter for Use in Animal Studies. NM 24 01 00.04.03, 4 June 1958.
3. Chemical Thermodynamics and Molecular Mechanism of Muscular Contraction. NM 01 01 00.01.02, 5 June 1958.
4. Radiation Biology: Definitions, Basic Manifestations, and Concepts. Lecture and Review Series No. 58-2, 30 June 1958.
5. Short and Long-Term Observations Concerning the Effect of Homologous and Heterologous Cell-Free Spleen Extracts on Radiation Mortality in Mice and Guinea Pigs. Lecture and Review Series No. 58-4, 10 July 1958.
6. Thermal Radiation Burns in Rabbits. II. Quantitative Studies Relating Radioactive Phosphorus Uptakes to Healing Rate. NM 007 081.03.04, 11 July 1958.
7. Labilization of Ester Bonds in Aminocyclitol Derivatives. I. Derivatives of Myo and Seyllo Inositol and of Streptamine. NM 02 02 00.01.08, 14 July 1958.
8. Effect of Growing on Experimental Granuloma Formation in Mice. NM 24 01 00.04.04, 25 July 1958.
9. Current Methods and Techniques in the Preparation and Microradiography of Mineralized Tissues. Memorandum Report 58-6 related to NM 71 01 00.06, 25 July 1958.
10. A Study of Some Effects of Gamma Radiation on the Adults and Eggs of Aedes Aegypti. NM 52 01 00.05.01, 29 July 1958.
11. Inhibition of Blood Digestion in Mosquitoes by Cations, and Cation-Antibiotic Mixtures. NM 52 07 00.01.01, 29 July 1958.

Naval Dental Research Facility, Great Lakes, Ill.

1. Clinical Evaluation of Analgesic Drugs. NM 75 03 27 01, June 1958.
2. Reviews of Naval Dental Research at Great Lakes 1953 - 1958.

Naval Medical Field Research Laboratory, Camp Lejeune, N. C.

1. An Electrophoretic Study of the Antibody Production in Rabbits Immunized Against Rattlesnake Venom. NM 51 03 09.1.1, July 1958.

Naval Medical Research Laboratory, Submarine Base, New London, Conn.

1. Some Correlates of Disqualification in the Submarine Service. Report No. 2, Subtask No. 1, NM 23 02 20, 30 August 1958.

Naval School of Aviation Medicine, NAS, Pensacola, Fla.

1. Relationships Among Three Types of Response Sets. Report No. 15, Subtask No. 1, NM 16 01 11, 1 July 1958.

Naval Medical Research Unit No. 2, Taipei, Taiwan

1. Acquisition of Intestinal Protozoa and Helminths by Young Children in a Typical Village of Lower Egypt. NM 52 15 02.1.4, July 1958.
2. Intestinal Protozoans and Helminths in Americans Residing in Southern Taiwan (Formosa). NM 52 11 02.1.2, September 1958.
3. Intestinal Protozoa and Helminths in the Peoples of Western (Anatolia) Turkey. NM 52 15 02.1.2, September 1958.
4. Development of the Cercariae of *Fasciola Gigantica Cobb* 1855 with Emphasis on the Excretory System. NM 52 15 02.1.1, September 1958.
5. *Schistosoma* Sp. in Shrews in Lower Egypt. NM 52 02 02.1.2, Sept., 1958.
6. Records of Trematodes Collected in Turkey with the Descriptions of New Species in the Families Lecithodendriidae and Plagiochiidae. NM 52 15 02.1.3, September 1958.
7. Relationship of Temperature to Mulloscicidal Activity. NM 52 02 02.1.1, September 1958.

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BUMED NOTICE 6750

17 October 1958

From: Chief, Bureau of Medicine and Surgery  
To: Ships and Stations having Dental Officers

Subj: Conversion of dental operating units to higher speed operation

This notice announces continuation, in fiscal year 1959, of the program to convert dental operating units to higher speed operation; and furnishes information, guidance, limitations, and instructions relative to procurement of nonstandard items required for conversion.

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BUMED INSTRUCTION 6730.1A

21 October 1958

From: Chief, Bureau of Medicine and Surgery  
To: Ships and Stations Having Medical/Dental Personnel  
  
Subj: Noise protection ear plugs, procurement and fitting of  
  
Ref: (a) NMMO System Instruction 4235.1

This directive promulgates information concerning procurement, distribution, and fitting of noise protective ear plugs by MD personnel. BuMed Inst. 6730.1 is superseded. It is advised that Medical officers recommend routine use of ear plugs to all personnel exposed to hazards of excessive noise and vibration insofar as use of ear plugs does not interfere with safe and efficient performance of duties.

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BUMED INSTRUCTION 6700.1A

24 October 1958

From: Chief, Bureau of Medicine and Surgery  
To: Ships and Stations having Medical/Dental Personnel  
  
Subj: Medical and dental equipment; maintenance and repair program

This instruction provides information concerning the employment of Medical Repairmen (MRM) and Dental Repairmen (DRM), and furnishes instructions relative to the procurement of repair parts and tools. BuMed Instruction 6700.1 is canceled. Detailed instructions relative to proper operational maintenance, care, and storage are furnished with all special equipment. Pertinent information should be abstracted from these instructions into easily readable form which operating personnel should be required to follow.

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Use of funds for printing this publication has been approved by the Director of the Bureau of the Budget 19 June 1958.

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**DENTAL****SECTION**

Examination Program of the American  
Board of Prosthodontics

The 1958 Report of Officers and Councils of the American Dental Association contains the following information regarding the inclusion of fixed partial dentures within the purview of the American Board of Prosthodontics for the purpose of examination and certification.

The Council on Dental Education of the American Dental Association has developed a plan whereby the American Board of Prosthodontics will continue as a specialty board with the provision that it examine qualified candidates in the broad area of prosthodontics, as now defined, to include complete denture prosthesis and partial denture prosthesis (both fixed and removable). This plan was developed to serve as a pattern when and if other related areas in the field of prosthodontics might be eligible for inclusion and when and if it might be found desirable to combine other areas into one specialty board.

The Council's philosophy is that the dental profession should not be oversegmented, but this philosophy does not arbitrarily place any specific limit on the number of dental specialty areas. Every effort will be made to give recognition to those areas of dental practice which meet the definition and requirements set forth in the "Requirements for the Approval of Examining Boards in the Dental Specialties."

The Council's philosophy is that the scope of any specialty should be sufficiently broad to include the various elements of special competence which are encompassed by that specialty area and, in this instance, that recognition of a specialist in the field of prosthodontics should attest to his skill, knowledge, and competence in the broad area of prosthodontics, not in one specific sub-area.

Scope of Examinations Given by the American Board of Prosthodontics. The American Board of Prosthodontics will examine candidates in the broad area of prosthodontics which shall include complete denture prosthesis and partial denture prosthesis (both fixed and removable). As indicated in a later section on the "transition period," the Board will be permitted, for a period of 4 years (ending December 31, 1962) to examine candidates by giving special attention to their specific areas of interest and competence. After this 4-year period, all candidates will be expected to have special competencies in the broad area of prosthodontics.

Certificate of a Diplomate. All diplomas or certificates will indicate that the individual is a diplomate of the American Board of Prosthodontics, thereby attesting to his special knowledge and skills in the broad area of prosthodontics. There will be no notation on the certificate of special qualifications in a sub-area.

Transition Period. There will be a transition period of approximately 4 years terminating on December 31, 1962, after which all qualified applicants will be examined in the broad area of prosthodontics. During this transition period, all individuals who meet the requirements for examination in the broad area of prosthodontics will be given the same basic science and theory examination. During this period, the examiners will, through their examinations, give special emphasis to those areas which in the judgment of the examiners are appropriate for the candidate as indicated by his credentials and his particular areas of practice, experience, and education.

During the transition period, those candidates who represent the newly added area of competence that has not been previously evaluated by the Board, namely, those in fixed partial denture prosthesis, will not be required to have had 2 years of formal education. Those accepted without this formal period of training, as defined by the Council's requirements, will be expected to have had 10 years of experience as specified by the Council's requirements under the "waiver" provision, the major portion of which must have been in the area of special competence.

It should be further explained that during this interim or transition period all who make application because of their primary interest in complete denture prosthesis or removable partial denture prosthesis must meet all existing requirements of the Board and the Council; these requirements include a minimum of 2 years of formal education and an additional 3 years of practice devoted principally to the specialty. It is not possible for the Board to exercise interpretations beyond those stated above. It should also be explained that during this transition period the Board may examine applicants in the area of fixed partial denture prosthesis if the applicants have had 2 years of formal education plus 3 years of additional practice devoted primarily and principally to the specialty area.

Examiners of the American Board of Prosthodontics. In addition to the regular members of the Board Examiners, consultants may be called upon to assist in the development and administration of the written and practical examinations. These consultants shall be selected from those who are diplomates of the American Board of Prosthodontics. However, during at least part of the transition period, it will be necessary and desirable for the Board to utilize personnel who are not diplomates, but who are judged by the Council to be especially competent in the field of prosthodontics with special competence in the area of fixed partial denture prosthesis so that at least two of these individuals may be used by the Board in its first examination to be announced.

"Grandfathers" or Founders. Eligibility for certification will be based on examination and upon other criteria of eligibility as set forth by the Council's "Requirements for the Approval of Examining Boards in Dental Specialties," and by other parts of this report.

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BuMed Instruction 1520.2F - Graduate and postgraduate training for officers of the Dental Corps, U. S. Navy and U. S. Naval Reserve, on active duty. This instruction supersedes and cancels BuMed Instruction 1520.2E. The revised instruction has been modified to conform with changes in the Manual of the Medical Department, Chapter 6. The revision includes the changing of "Advanced Prosthodontic Training" to "Residency Training in Prosthodontics" in recognition of approval by the American Dental Association of the programs at the U. S. Naval Dental School, National Naval Medical Center, Bethesda, Md., and the U. S. Naval Station, Treasure Island, San Francisco, Calif.

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BuMed Instruction 6750.2C - Dental outfitting materiel, procurement procedure. This instruction supersedes and cancels BuMed Instruction 6750.2B. The new revision authorizes the procurement of materiel for expansion of dental facilities, when equal to initial outfit, without submission of numerous requisitions.

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## RESERVE SECTION

### New Department Added - ROPRA Now Called RORA

When a classification department was added to its mission, the Reserve Officer Performance Recording Activity (ROPRA) changed its title to Reserve Officers Recording Activity (RORA).

RORA's classification department will be of considerable importance to inactive USNR officers and retired USN officers in the event of mobilization. It will have the task of evaluating and classifying naval and civilian

qualifications of all officers on inactive duty. The new department will also help select qualified personnel to fill specialized billets and will provide qualification information for mobilization planning and training needs to the various offices of the Navy Department. These functions were previously carried out at BuPers in Washington.

RORA will continue to handle Reserve officers' records as in the past. Officers should direct their requests for annual statements of satisfactory Federal service to the Officer in Charge, Reserve Officers Recording Activity, Naval Personnel Center, Omaha 11, Neb.

(The Naval Reservist, September 1958)

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Promotion Zones and Convening Dates  
of Selection Boards

Promotion zones as indicated in the following table reflect date of rank of junior officer to be considered:

For Pro- motion to:	CDR	LCDR	LT	LTJG	CONVENING DATE OF SELECTION BOARD
CAPT	7-01-51				24 February 1959
CDR		1-01-55			24 February 1959
LCDR			7-02-54		28 April 1959
LT				12-30-56	2 June 1959

Note: Reserve Ensigns are promoted in accordance with the provisions of BuPers Instruction 1412.10A

Eligibility. Reserve officers, both men and women, in the grades of lieutenant (junior grade) and above within the above established promotion zones will be considered provided they are:

1. TAR officers on active duty, or
2. On active duty but have not been considered by an active-duty board meeting in fiscal year 1959, or
3. Reserve officers on inactive duty, in an active status, and who have earned at least 12 retirement points during fiscal year 1958. (Officers released from active duty on or after 1 July 1955 are not subject to these retirement point requirements.)

Warrant officers and chief warrant officers of the Naval Reserve will be considered for promotion by a selection board tentatively scheduled to convene on 12 May 1959, and will be eligible for consideration for promotion if they earned 12 retirement points during fiscal year 1958, and on 30 June 1960, will have completed the following number of years' service in present grade:

WO, W-1 to CWO, W-2 -- 3 years  
CWO, W-2 to CWO, W-3 -- 6 years  
CWO, W-3 to CWO, W-4 -- 6 years

Nurse Corps officers of the Naval Reserve are eligible for consideration for promotion when they are senior to the junior officer of the same grade of the Nurse Corps on active duty on the lineal list of the Navy who has been selected for promotion. Accordingly, promotion zones for Reserve officers of the Nurse Corps will be established upon final approval of the fiscal year 1959 lineal list selection boards for Nurse Corps officers.

Fitness Reports. Officers who are within the promotion zones should insure that fitness reports for training duty and/or annual fitness reports and annual qualification questionnaires covering periods ending prior to convening dates are submitted to the Bureau of Naval Personnel in time to be included in the officers' records when presented to the selection board. Special fitness reports are not required. (BuPers Note 1412 of 18 Oct 1958)

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#### Publication Available to Ensigns 1915

Third and fourth year medical students commissioned as Ensign 1915 USNR officers are eligible to receive gratis the monthly publication of the United States Armed Forces Medical Journal. Requests for this professional medium should be submitted to the Chief, Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C.

The USAFM Journal's Foreword is reprinted herewith as being descriptive of its purpose:

"The United States Armed Forces Medical Journal is the medium for disseminating information of administrative and professional interest to all medical personnel of the Department of Defense. The Assistant Secretary of Defense (Health and Medical) and the Surgeons General of the several services invite all Medical officers, Dental officers, Medical Service Corps officers, Nurse Corps officers, and officers of the Veterinary Corps of the Armed Forces, and the medical consultants of the Army, Navy, and Air Force to submit manuscripts for publication in this Journal."

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## PREVENTIVE MEDICINE SECTION

### — Penicillinase-Proved Allergy to Penicillin in Poliomyelitis Vaccine

Six reactions in patients given injections of poliomyelitis vaccine were considered to be due to traces of penicillin present in the vaccine because each patient had had a previous similar reaction known to be due to penicillin allergy. The reaction after use of poliomyelitis vaccine duplicated the previous penicillin reaction. Each patient obtained rapid clearing after being given a penicillinase injection (which would have no effect on anything but penicillin) and no recurrence followed subsequent administration of another brand of vaccine containing all the same allergens except penicillin.

Patients with previous penicillin allergy should receive penicillin-free vaccines. If this is impossible, penicillinase should be given prophylactically preceding the vaccine injection. Before the use of penicillinase, a specific cause for reactions to poliomyelitis vaccine was hard to prove. Such reactions could be due to chance, to psychic stress from the injection, to traces of a contaminant in the syringe, to intercurrent illness, or to a constituent of contaminant of the vaccine. The vaccine contains monkey protein, horse serum, formaldehyde, preservatives, and other antibiotics—all potential causes of reaction. (Author's Summary, Zimmerman, M. C., Penicillinase-Proved Allergy to Penicillin in Poliomyelitis Vaccine: J. A. M. A., 167: 1807-1809, August 9, 1958)

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### Changing Patterns in Pesticides

Prior to World War II, pest control was a less complicated procedure owing in part to the small number of chemicals which were available for use. For example, in insect control, arsenicals, some of the fluorides, nicotine products, phosphorus, and pyrethrum or rotenone were the most frequently used materials; for rodent control, white arsenic, barium carbonate, thallium sulfate, zinc phosphide, phosphorus, cyanides, carbon disulfide, methyl bromide, strychnine, and red squill were known; in control of fungi, sulfur, formaldehyde, some copper salts, and a few mercurials

were used; and for weeds, arsenites, carbon disulfide, sodium chlorate, salt, and a few others were reasonably effective. Some minor questions were raised about possible adverse effects, but most research attention was centered on finding new chemicals which would do better or cheaper jobs of pest control or in improving the formulas for the older ones. This pattern is built around the principle that the form of life to be controlled has been shown to be detrimental to man's well-being and worthy of destruction with the most effective procedures which can be found. In short, it is the pattern which supports the idea that man is truly at war with the insects, fungi, and rodents which transmit diseases, destroy his crops and forests, infest and damage his homes, or contaminate his food.

It is a most convincing pattern for many conscientious guardians of health, food, and property, and it is natural for a public health worker to appreciate the value of the pesticide which he can use to reduce the threats of malaria or bubonic plague; for an agriculturalist to praise the pesticides which will protect the quality and increase the yields of his crops; and for the home owner to be enthusiastic about the materials which will protect his property best against termites, decay, cockroaches, ants, and rats and mice—to mention only a few of the household pests.

With the outbreak of war in Europe in 1939, many laboratories in the United States began to anticipate an emergency changing pattern in pesticides, because in several areas of pest control the most useful chemicals came from abroad. This was particularly true in the control of rodents, because red squill, strychnine, and thallium were all imported. This meant that a search for new products which could be synthesized in this country would soon become essential. In 1941, because of growing military demands, this pattern was crystallized rapidly and a tremendous increase in the search for new synthetic chemicals was stimulated. Within a few years, alphanaphthylthiourea, sodium fluoroacetate (1080), and warfarin were discovered and became the leading rodent control chemicals.

In the field of insect control, this started the "DDT" age in which we are now living. The discovery that dichloro-diphenyl-trichloroethane was a most effective insecticide set a multitude of chemical laboratories to work and the list of chlorinated hydrocarbons made available for testing as possible pesticides soon included such names as benzene hexachloride, toxaphene, heptachlor, chlordane, lindane, aldrin, dieldrin, strobane, methoxychlor, and endrin. As the spectacular research in this field progressed and certain medical and health workers began to ask logical questions about the potential dangers of the many new chemicals, the old pattern of seeking performance alone appeared to be less clear-cut than before and a new trend began to emerge—the trend to consider the safety of the candidate materials as an essential part of their evaluation.

Further interest in the safety factor was stimulated by the discovery of the pesticidal value of the class of chemicals called "organic phosphates."

Parathion was the first pesticide in this category to gain accepted use in this country. As with DDT, however, parathion soon had a host of competitive products among which were tetraethyl pyrophosphate (TEPP), systox, malathion, Phosdrin, and thimet.

As these two new classes of chemicals reached widespread use, medical men began to express increasing concern over the possible effects which they might have on humans who were exposed repeatedly to them either by ingestion, inhalation, or skin absorption. Searching questions were raised for which complete answers were lacking and the recognition that such a situation needed changing started an entirely new pattern. This pattern was based on the principle that the user of a pesticide should know its potential hazards and how to protect himself, other humans, and valuable animals against injury, and that the public should be protected against dangerous residues in and on foods.

Operating under the provisions of the Federal Insecticide, Fungicide, and Rodenticide Act which became law in 1947, the U.S. Department of Agriculture requires precise instruction on the labels of all pesticides offered for interstate shipment which will be adequate to protect the user when they are followed and—acting under the procedures outlined in the Pesticide Chemicals Amendment to the Federal Food, Drug, and Cosmetic Act—the Food and Drug Administration establishes the levels of residues of pesticides which will be safe when consumed by humans or, in many cases, by animals, and sets tolerances on the various raw agricultural commodities on which the chemicals are proposed for use.

What effect has this added control had on the changing patterns of pesticides? First, it has divided the concept of safety into two main parts: operator protection against acute skin absorption and inhalation, and public protection against long-continued or "chronic" ingestion; and it has started a number of trends in the search for new pesticides depending upon the end uses of the material. The company producing the chemical and the research agencies testing it must undertake work to determine the following attributes:

1. Effectiveness against at least one pest of economic importance
2. Precautions needed to insure safe handling
3. Toxicity from acute and chronic exposures
4. Persistence of residues and safe tolerances

A new product must be effective or it will be set aside, but under the new pattern it does not necessarily have to be superior to its competitors in performance to justify further study as would have been required in the past. It may be less effective, but if it is safer to handle or leaves a less persistent residue, it will deserve the added scrutiny it will get.

The new revolutionary pattern is beginning to take form, but is not yet firm enough to be adopted by all manufacturers nor does it dominate the thinking of all researchers who are seeking the means to eradicate disease

vectors or other serious pests of civilian or military importance. The tendency to employ highly toxic products for uses where definite hazards are recognized is based on the factor of "calculated risk"—a pattern which will probably dominate much of pesticidal usage for a long time to come. For just as the physician prescribes and administers potent drugs which could kill his patient if misused to fight the disease which threatens life or health so the user of a pesticide takes his chances with the product he applies in order to destroy the pest. There is much that can be improved in the handling of poisons of all kinds—drugs, pesticides, and hazardous household products alike—and conscientious efforts are being made by many interested groups to find the best ways to speed that improvement. A recent move has been the establishment of Poison Control Centers throughout the country (See Medical News Letter, Vol. 31, No. 5, pps. 21-26, 7 March 1958). These Centers are providing a needed service to physicians in the handling of accidents from poisons including pesticides. When, through cooperation between the chemical industry and research, legislative, and regulatory agencies of Government, laws are passed that place safety considerations on a par with, or even above, performance factors in judging the acceptability of a pesticide, great progress will have been made.

Added developments in recent months may forecast still another pattern. The adoption of radioactivity to destroy the ability of certain insects to reproduce has disclosed a new pest control procedure suitable for trial with species having specific life habits which make this system feasible. The distribution of certain specific bacterial cultures in dusts over crops infested with susceptible insects and the use of predatory or parasitic insects to destroy unwanted species are procedures being given further careful study because they will tend to replace chemical controls if successful and thereby reduce residue problems.

On the chemical front there are: (1) intensive studies to protect live-stock against specific insect pests through internal doses of pesticides which will be effective, but will leave no residues in the meat when eaten; (2) developments for treating poultry with antibiotics to preserve the meat for a longer period; (3) trends to protect humans, animals, and property through the use of repellents which serve to drive the pest away rather than to destroy it.

Some of these patterns have been in use for years, but others are as new as the most recent legislation, the Miller Pesticide Chemicals Amendment of 1954. With the authority in the laws now on the books governing pesticides and with the growing knowledge of toxicity and tolerances, feelings of fear should change to respect. As this occurs, pesticides can be used more effectively and with greater safety. When more is learned about both long-term and acute reactions to pesticides, greater advantage can be taken of their values without too much risk. The patterns of use have changed a great deal in the past 10 years. How much more they will

change in the next decade cannot be foretold, but it is reasonably safe to prophesy that the pattern in which the performance of a pesticide was the dominating factor of importance has been replaced by one in which performance shares the emphasis with factors of safety. It is likely that this trend will dominate the development and use of pesticides for many years—which is as it should be when public safety is at stake. (Ward, J.C., M.Sc., Changing Patterns in Pesticides: Arch. Indust. Health, 18: 134-137, August 1958)

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#### Epidemiological Studies of Tuberculin Sensitivity

Preliminary results are reported from the most recent in a series of epidemiologic studies on the specificity of skin sensitivity to tuberculin in human beings. Patients in tuberculosis hospitals and healthy young Navy recruits were tested with mammalian tuberculin (PPD-S) and with purified protein derivatives prepared from two types of atypical acid-fast organisms recently isolated from patients with clinical disease resembling tuberculosis. One of the new antigens, PPD-B, was prepared from a nonphotochromogen isolated at Battey State Hospital, Georgia; the other, PPD-Y, was prepared from the "Yellow" bacillus, a photochromogen isolated in Kansas City. Dosage for all 3 antigens was set at 0.0001 mgm.

Tests with PPD-S and PPD-B given at Battey Hospital showed that almost all patients infected with typical tubercle bacilli had definite, fairly strong reactions to PPD-S and a smaller or no reaction to PPD-B. Patients infected with the "Battey" organism had larger reactions to PPD-B than to PPD-S. Thus, comparative testing provided a way to separate the tuberculin sensitivity produced by the Battey organism from that produced by typical tubercle bacilli.

Results of testing with PPD-S and PPD-Y in patients at the Suburban Cook County Hospital, Illinois, some infected with typical tubercle bacilli and some with the Yellow bacillus, showed that the sensitivity produced by these two organisms is too similar to be distinguishable by comparative testing.

Testing of normal healthy populations with PPD-S and other antigens has been most extensive in connection with the routine skin testing of Navy recruits now being carried out cooperatively by the U.S. Navy and the Tuberculosis Program of the Public Health Service. Since December 1957, recruits coming to the Great Lakes Training Center and, since April 1958, recruits coming to the San Diego Training Center have been included in the program. Among the Navy recruits, the frequency of reactions to PPD-B ranged from around 30% in lifetime residents of the northeastern part of the country to about 65% in the southeast. Reactions to PPD-S ranged from

6 to 9% and also increased in frequency from north to south, the increase being entirely accounted for by an increase in the small 6- 11-mm. reactions. If, as found in patients, reactions to PPD-S equal to or larger than the corresponding reaction to PPD-B are interpreted as specific for tuberculous infection, and if reactions to PPD-S smaller than to PPD-B are interpreted as nonspecific for tuberculous infection, then geographic variations in the frequency of small reactions to PPD-S can be entirely accounted for by variations in the proportion of nonspecific reactions. When such reactions are excluded, the frequency distributions of reactions to PPD-S for recruits from different geographic areas are similar to one another and also to the distribution of reactions found among tuberculous patients.

These findings constitute striking confirmation of the hypothesis that a varying proportion of the small, so-called "positive" reactions to the 5 TU dose of tuberculin are not indicative of tuberculous infection. Instead, they represent sensitization by other organisms of which the Battey organism appears to be one. This dilution of small specific reactions by nonspecific reactions may inflate estimates of the prevalence of tuberculous infection by as much as 100% or more in some geographic areas. It may also account for the lower risk of developing tuberculosis associated with small, as compared with large, reactions to the 5 TU test as well as for the unusually high and unrealistic conversion and reversion rates reported from some geographic areas. (Edwards, L. B., Palmer, C. E., Epidemiologic Studies of Tuberculin Sensitivity: Am. J. Hygiene, 68: 213-229, September 1958)

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Permit No. 1048

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